

ARTICLE IX.—*On the Therapeutics of Aloin.* By WILLIAM CRAIG, M.D., F.R.S.E., F.R.C.S. Ed., etc., Lecturer on Materia Medica, Edinburgh School of Medicine.

(Read before the Medico-Chirurgical Society of Edinburgh, 7th February 1877.)

ALOES, the *aloc* of the Pharmacopœia, is the inspissated juice of the leaves of various species of Aloe. Although it has been used in medicine for upwards of two thousand years, our knowledge of the chemistry of this drug is still imperfect. As yet only two bodies have been isolated, and both of these have been discovered by the Messrs Smith of this city. In 1851 they discovered in Barbadoes aloes a crystalline body, to which they gave the name *aloin*, because by them it was supposed to be the active principle of the drug. Besides aloin, aloes contains a volatile oil, to which the drug owes its peculiar flavour. This oil was first isolated by the Messrs Smith in 1872. It is a pale yellow, mobile liquid, with a resemblance in taste and smell to the oil of peppermint. It differs from the oil of peppermint both in its specific gravity and in its boiling point. It exists in small quantity in aloes, only one fluid ounce being obtained from 400 lbs. of aloes. Aloes also contains a considerable amount of a substance called *resin of aloes*. This resin deposits from a decoction of aloes as it cools. It is partially soluble in rectified spirit, about 85 per cent. being dissolved by spirit. Resin of aloes leaves, when burnt, a considerable amount of ash. These are the most important constituents of aloes. It is to the first of these constituents that I mean specially to direct your attention; but, as the resin of aloes generally contains a variable amount of aloin, I wish to make a few remarks on the action of this resin. In many works on materia medica this resin is spoken of as *modified aloin*, and consequently partaking more or less of the actions of that substance. By others it is spoken of as a very active substance, if not the active principle of aloes. Others, of whom I am one, believe that it is wholly inert. Chemically, it is very different from aloin, inasmuch as it leaves a considerable amount of ash when burnt, whereas aloin leaves no ash. Physiologically it is also very different from aloin. It was long supposed that the resin was the cause of the griping of aloes. The experiments of Dr Farre, Dr Garrod, and Dr Harley, have shown this theory to be utterly untenable; and in a series of experiments I performed in 1874, I was enabled fully to confirm their opinion. I found that even in doses of twelve grains it failed to produce griping. Unless this resin is prepared with extreme care, it will contain an amount of aloin. This, I believe, to a great extent accounts for the difference of opinion regarding the activity of this substance. I performed, three years ago, a series of experiments with this substance

upon rabbits, with the view of ascertaining the action of the resin of aloes, and afterwards confirmed my conclusions by experiments on the human subject; and the conclusion to which I came is thus expressed in the *Edinburgh Medical Journal* for June 1875:—"The resin of aloes, when thoroughly exhausted of aloin, possesses no purgative properties." I still adhere to that opinion. In one of the best manuals of materia medica in this country, and one of the most recent, I mean the very excellent edition of Royle's *Materia Medica* by Dr Harley of London, reference is made to my paper on this subject, and Dr Harley states that his observations do not support my statement, inasmuch as he found that two grains of resin mixed with three grains of soap purged him freely. It might be a fair question for discussion, what effect the soap had in producing this purgation. In experimenting with cathartic substances we should never use soap, which is itself laxative. Gentian would be a far better substance to use in such cases. I have already mentioned that it is extremely difficult entirely to exhaust the resin of aloin, and I have the authority of Mr Smith to say that the resin of aloes with which Dr Harley experimented, and which was supplied by the Messrs Smith, did contain aloin. In my first experiments with the resin of aloin I obtained similar results, and on communicating these results to Mr Smith, he immediately examined the resin, and found that it contained a small amount of aloin, and afterwards prepared some which he believed to be as nearly exhausted of aloin as resin can well be; and when I experimented with this resin, I found it perfectly inert, even in doses of twelve grains. The Messrs Smith have since supplied Dr Harley with this carefully prepared resin, but what is the result of Dr Harley's experiments with this resin I am not aware. Dr Farre of London gave to patients doses of three grains of resin of aloes, and says that he found it almost inert, and that it seldom produced any evacuation. I believe that any little purgative effect which he observed might have been due to the aloin it contained.

I come now to speak more at length regarding *aloin*. This I believe to be the active principle of aloes. Aloin exists in all kinds of aloes. Good Barbadoes aloes contains about 25 per cent. of aloin. Aloin occurs in long yellow acicular crystals, transparent and doubly refracting. It is sparingly soluble in cold water, but freely in ether and chloroform. It is an oxidized hydrocarbon, having the formula $C_{16}H_{18}O_7$, according to some chemists, differing, however, in different species of aloes in the amount of water it contains. According to Dr Tilden, the aloin obtained from Barbadoes aloes contains three atoms of water; that from Socotrine aloes, one atom of water; whilst that from Natal aloes is anhydrous. These various kinds of aloes differ also in their solubility and form of their crystals, but are believed to have the same physiological actions. They are generally distinguished as Bar-

baloin, Socaloin, and Nataloin, according as they are obtained from Barbadoes, Socotra, or Natal aloes respectively.

Aloin is the only active principle contained in aloes, and possesses all the properties of the crude drug, and is free from griping. In small doses it is a tonic. It assists digestion. It gives tone to muscular tissue, and is thought to exert a special influence on the liver. In larger doses it is a purgative, acting specially on the large intestine. It increases the intestinal secretions, and also the peristaltic action of the bowels. It is believed also to stimulate the uterus, and hence is useful in certain sluggish states of that organ. The sulphate of iron, and other substances, increase its purgative action. I have experimented largely with aloin on rabbits, and have always found it an active aperient, and have given it almost daily to patients for several years, and have found it a trustworthy and beneficial medicine. Although aloin has now been used in medicine more or less for a quarter of a century, nevertheless there are still held most erroneous views regarding its actions and uses. Even so recent as February 1876, we find an anonymous writer in the *Edinburgh Medical Journal* thus writing regarding aloin:—"Dr Craig insists strongly on the superior efficacy of aloin over aloes in doses of $\frac{1}{2}$ to one grain, the dose of aloes being stated as two to six grains; but every practitioner is aware that, for most purposes, a much smaller dose is sufficient, $\frac{1}{2}$ to one grain generally fulfilling all its indications. Hence it is very doubtful if aloin is more powerful or even equal to good Barbadoes aloes." The above was evidently written by one who was ignorant of the very first principles of therapeutics, and he has been led to draw a most illogical conclusion from false premises, showing that his logic was as deficient as was his knowledge of drugs. This unknown author accuses me of stating the dose of aloes as two to six grains—that being the dose given in the British Pharmacopœia and in all the best works on materia medica—and what I am bold to affirm is the correct dose of aloes. The merest tyro in therapeutics knows that there are instances in which smaller doses than those given in the British Pharmacopœia will suffice for our patients; but no sane person ever argued from this that the doses given in the British Pharmacopœia are incorrectly stated. Every practitioner knows that constipation, the disease for which aloes is most frequently given, may exist in any degree, from the merest tendency to costiveness up to complete stoppage of the bowels; and every practitioner knows that the quantity of medicine will vary accordingly. It is quite true that less than two grains of aloes will frequently suffice, but it is equally true that in such cases less than $\frac{1}{2}$ grain of aloin will be sufficient. In such cases it will be found that $\frac{1}{8}$ to $\frac{1}{4}$ grain of aloin will be all that is required. The best authorities have come to the conclusion that aloin is at least two or three times as active as good aloes.

Mr Finlay Dun, in his excellent work on Veterinary Medicines, states as the result of his experiments, that two drachms of aloin acted on "horses several hours earlier, without impairment of appetite or spirits, and with the certainty and effect which usually follow six drachms of Barbadoes aloes." He also mentions that Mr Dollar of London, as the result of his experiments, "concludes that, comparing aloin with the crude drug, little less than half the quantity acts in horses with more certainty and equal effect." Dr Harley of London states, in the last edition of Royle's *Materia Medica*, that "the action of aloin is at least twice as strong as that of the best aloes." He further states that, as the result of several experiments, he has come to the following conclusions:—

"1. The cathartic action was uniform, rather more speedy than that of crude aloes, and unattended by griping.

"2. The average dose for a strong adult male is about $1\frac{1}{2}$ grain, which usually causes two or three copious evacuations. $2\frac{1}{2}$ grains were always followed by powerful catharsis, producing five or six evacuations."

Even Dr Tilden of London, a chemist who has devoted much attention to the constituents of aloes, is rapidly advancing in his views regarding the activity of aloin. So late as 1870, we find Dr Tilden maintaining that "the purgative property of aloes is not due to aloin, and that the active constituents of aloes is still unknown." In 1876, however, we find him stating that "Barbaloin in doses under two grains frequently produces some slight laxative action. Two grains cause a decided effect, never, however, amounting to complete purgation." He further admits that aloin causes less griping than aloes. Dr Tilden, in conjunction with Mr Dobson, F.R.C.S., performed some experiments with aloin in the Bristol Hospital, and their observations have been recorded in the *Medical Times and Gazette*, 12th August 1876, and in the *Pharmaceutical Journal* for 19th August 1876. They experimented in fifty cases, mostly adult males, and they state that they never gave Barbaloin in more than two-grain doses. They have clearly demonstrated that aloin is possessed of aperient properties, and that it causes less griping than the crude drug. After quoting from my paper on aloin in the *Edinburgh Medical Journal* for June 1875, they state that, "so far as their observations go, they do not fully agree with the experience of Dr Craig." Possibly this may, to some extent, be accounted for by the fact that they had not tried it in a sufficient number of cases; or, at all events, in cases suitable for the administration of aloes. It appears to me that some of their own conclusions are altogether untenable, and are inconsistent with other parts of their paper. Be it borne in mind that in no case did they give more than two grains of Barbaloin, and contrast this with the fact, that they state in another portion of the paper that "it did not appear to them that the crystalline

principle was more potent than a similar dose of aloes." What would we say of conclusions drawn regarding the action of Barbadoes aloes if no dose higher than two grains had been given? Is not the very fact that they did not give Barbaloin in larger doses than two grains, to prove its purgative properties, an indication that they believed it more active than Barbadoes aloes?

That aloin possesses purgative properties there cannot be the least shadow of a doubt. I am not aware of any good authority who denies this; and, as the results of my experiments on rabbits, I have come to the conclusion that it is the only active principle contained in aloes. I have, during the past three years, prescribed aloin almost daily, and have always found it a reliable and valuable medicine. It is chiefly in chronic constipation that I prescribe aloin. In habitual constipation it is one of the very best medicines we possess. To persons of a sedentary occupation, with constipation and general sluggishness of the bowels, the administration of aloin in small doses will generally be very beneficial. Aloin being comparatively slow in its action, is not suited when we wish to empty the bowels freely and quickly; in such cases it is not to be compared with such vegetable purgatives as scammony or jalap, nor is it equal to elaterium or gamboge in dropsies; but it is far superior to any of these substances in chronic constipation with sluggishness of the liver and other abdominal viscera. In such cases I generally give it in doses of $\frac{1}{8}$ to $\frac{1}{2}$ grain, in pill, combined with iron, and in all such cases I prescribe the dried sulphate of iron, which is the best of all the ferrous sulphates for forming pills. I frequently give quinine in the same pill, combined with extract of nux vomica, and sometimes capsicum or myrrh. The following pill I have found very valuable:—

R Aloin., gr. $\frac{1}{4}$.
Ferri sulph. exsic., gr. iss.
Quin. sulph., gr. i.
Capsici, gr. $\frac{1}{4}$.
Extract. nucis vomicæ, gr. ss.
„ Gentianæ, q. s. ut fiat pil.
Sig.—One pill two or three times a day.

The various constituents can be varied according to circumstances.

I would only add further, that there are few indications against the administration of aloin. I have given it in pregnancy and hæmorrhoids, and have never seen any bad effects follow. When my own observations are viewed in connexion with the researches of numerous experimenters in regard to the activity of aloin, I am forced to the conclusion that aloin is the only active principle contained in aloes, and is sufficient to account for all the purgative properties of that medicine.

That being the case, I cannot conclude without again express-

ing a regret (as I did in 1875) that in the "Addendum to the British Pharmacopœia of 1867," published in 1874, no mention is made of aloin. It ought to find a place amongst the medicines recognised in the British Pharmacopœia. It possesses the following advantages over the crude drug:—

1. Being uniform in strength, its dose can be accurately determined.

2. Its dose being $\frac{1}{8}$ to one grain (usually $\frac{1}{4}$ grain), it can easily be introduced into tonic pills without making these pills too large.

3. By using the active principle, we get rid of all impurities, which are so apt to cause griping.

Its uniformity in strength, the smallness of its dose, and the certainty of its action, should commend it to the favourable consideration of all medical practitioners.

Part Second.

REVIEWS.

Traité de la Diphthérie. Par. A. SANNÉ, Docteur en Médecine, Ancien Interne des Hôpitaux de Paris. Pp. 634. Paris: 1877.

(Concluded from page 830.)

THE portion of Dr Sanné's work which treats of the *etiology* of diphtheria begins with a condensed history of the principal epidemics which have prevailed in France and other countries since 1862. The author does not go back to earlier times, considering it unnecessary to reproduce well-known accounts of epidemics prior to that date. He refers to them, however, for purposes of explanation and comparison.

"In certain great towns—notably in Paris—diphtheria," says the author, "has become endemic. Since 1856 it has reigned continuously in that capital, with frequent exacerbations; as has been shown by discussions in the scientific societies, and by the reports of the Commission appointed to inquire into prevailing diseases. In England and in Germany its progress has been similar. In many localities, therefore, it is difficult to follow the advance of the disease and to study the conditions under which it has become developed. The necessary information on these points can only be furnished by epidemics. They enable us to investigate the influences of climate which preside over the hatching of diphtheria, and to inquire into its mode of transmission."



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